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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/583,329	06/16/2006	**Jaan Palgi**	1034456-000037	5095

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
05/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/583,329	PALGI ET AL.	
	Examiner	Art Unit	
	DAVID C. THOMAS	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *11-14 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,15 and 17-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed February 18, 2009 is acknowledged. Claims 1, 2, 4-6, 9, 10 and 15 (currently amended), claims 3, 7 and 8 (previously presented) and claims 17-23 (newly added) will be examined on the merits. Claims 11-14 and 16 were previously withdrawn.

Claim Interpretation

2. Prior to examination of the claims, the claims must first be construed. In claims 1, 5, 8 and 9, the term "complementary sequences" is used in regard to sequences of primers or probes that comprise specific SEQ ID numbers, "complementary sequences" thereof and/or functional fragments thereof. Since there is no strict definition of "complementary sequences" in the specification, for examination purposes, "complementary sequences" is interpreted as sequences that can hybridize under non-stringent conditions and therefore need not be fully complementary to their target sequences. For prior art purposes, this interpretation is extended to all of the dependent claims of claim 1.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

> granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-19, 15 and 17-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Doucette-Stamm et al. (U.S. Patent No. 6,800,744).

Doucette-Stamm teaches a diagnostic method for detecting and identifying bacterial species such as causing infections from a clinical sample (for overview, see Abstract and column 2, lines 17-20; bacterial species such as *Streptococcus pneumoniae* are responsible for a variety of different infections worldwide, column 1, lines 22-41), said method comprising:

a) amplifying DNA isolated from said clinical sample using a mixture of DNA primers that comprises sequences which hybridize with the sequences that originate from conserved regions of rpoB genes encoding DNA directed RNA polymerase [EC:2.7.7.6] subunit B of bacterial species causing infections (nucleic acids of the described sequences have utility as primers for amplification of target sequences, including those of S. *pneumoniae* and other *Streptococcus* species as well as other bacterial species such as *B. subtilis*, column 17, lines 55-59; targets include the RNA polymerase, subunit B gene sequences, see Table 2, columns 157 and 206 for examples of rpoB sequences), said sequences comprising SEQ ID NOS: 20 and 21 and/or complementary sequences (SEQ ID NOS: 20 and 21 are homologous to nucleotides 2803 to 2825 and 2915 to 2897, respectively, of SEQ ID NO: 1652 of Doucette-Stamm representing a fragment of the rpoB gene of *S. pneumoniae*),

b) contacting the amplified DNA with a desired combination of oligonucleotide probe sequences that hybridize under normal hybridization conditions with hyper-variable regions situated near said conserved regions of rpoB genes encoding DNA directed RNA polymerase subunit B of bacterial species causing said infections, said sequences being bacterial species specific under said hybridization conditions (nucleic acids of the described sequences have utility as probes for detection of amplified target sequences under stringent conditions, including those of S. *pneumoniae*, column 6, lines 51-55 and column 17, lines 12-20; Doucette-Stamm teaches nucleic sequences that would hybridize to such hypervariable regions, such as SEQ ID NO: 1652, which has homology to SEQ ID NO: 5 of the current invention, see below).

c) detecting the formation of a possible hybridization complex (probes for detection of target sequences by hybridization are associated with a label, column 10, line 66 to column 11, line 9, with detection including the capture of the target sequences on a solid support, column 11, lines 9-16).

With regard to claims 2 and 17, Doucette-Stamm teaches a diagnostic method wherein said bacterial species causing infections are bacterial species that cause human disease such as respiratory tract infections and ear, nose and throat diseases, (members of the *Streptococcus* genus such as *S. pneumoniae* are responsible for a variety of different infections worldwide, including meningitis, bacteremia and pneumonia, column 1, lines 21-30).

With regard to claim 3, Doucette-Stamm teaches a diagnostic method wherein said hyper-variable region is the hyper-variable region of the gene encoding the rpoB

protein of a bacterial species selected from *Haemophilus influenzae, Streptococcus pneumoniae, Streptococcus pyogenes, Pseudomonas aeruginosa, Staphylococcus aureus, Legionella pneumophila, Corynebacterium diphteriae, Mycoplasma pneumoniae, Escherichia coli, Moraxella catarrhalis* and *Neisseria gonorrhoeae* (nucleic acids of the described sequences have utility as probes for detection of amplified target sequences under stringent conditions, including those of S. *pneumoniae*, column 6, lines 51-55 and column 17, lines 12-20).

With regard to claims 4, 18 and 19, Doucette-Stamm teaches a diagnostic method wherein the length of oligonucleotide probe sequences used in step b) are 15-30 nucleotides long and are optionally labeled, or are 19-30 or 19-26 nucleotides long (detection probes used for hybridization assays under stringent conditions are preferably 20-40 nucleotides in length, column 6, lines 51-61; probes may be associated with a label, column 11, lines 1-6).

With regard to claims 5 and 20, Doucette-Stamm teaches a diagnostic method wherein said combination of oligonucleotide probe sequences comprises all or a portion of SEQ ID NOS: 1 to 19, and/or complementary sequences thereof (each oligonucleotide probe comprises sequences that include at least 20-40 consecutive nucleotides, column 6, lines 51-61; included are probes which can hybridize to SEQ ID NO: 3 or complementary sequences thereof, which is 67% homologous to SEQ ID NO: 1727 of Doucette-Stamm and to SEQ ID NO: 5 or complementary sequences thereof, which is 100% homologous to positions 2867-2888 of SEQ ID NO: 1652 of Doucette-Stamm in the rpoB gene of *B. subtilis;* these probes contain regions that can hybridize

to complementary regions of other members of SEQ ID NOS: 1-19 under non-stringent conditions).

With regard to claims 6, 21 and 22, Doucette-Stamm teaches a diagnostic method wherein said combination of oligonucleotide probe sequences is attached onto a solid support such as glass (nucleic acid probes may be immobilized on solid supports to function as a capture ligand, column 11, lines 6-12).

With regard to claim 7, Doucette-Stamm teaches a diagnostic method wherein the DNA isolated from the clinical sample in step a) is amplified using the polymerase chain reaction (PCR) (nucleic acids of the described sequences can serve as PCR amplification primers to create copies of S. *pneumoniae* nucleic acid, column 16, lines 27-29 and column 17, lines 55-64; and wherein the DNA amplified in step b) is contacted with the bacterial species-specific oligonucleotide probes attached onto a solid support (target nucleic acids, after PCR amplification, can be used in diagnostic assays such as by contacting with probes immobilized on a solid support, column 17, lines 37-40 and column 18, lines 6-8).

With regard to claims 8, 9 and 15, Drancourt teaches a diagnostic method wherein suitably labeled nucleotides are used in the amplification of DNA isolated from a clinical sample in step a) to generate a detectable target strand and wherein the amplified and optionally labeled target DNA in step b) is contacted with a solid support, preferably treated glass, on which all bacterial species-specific oligonucleotide probes of SEQ ID NOS: 1 to 19 or those shown in Table 3 and/or complementary sequences thereof have been attached (nucleic acids of the described sequences can serve as

PCR amplification primers to create copies of S. *pneumoniae* nucleic acid, column 16, lines 27-29 and column 17, lines 55-64; the nucleic acids may be modified with a label to provide a detectable signal, column 23, lines 52-56; amplification products may be contacted with solid support comprising capture probes, column 17, lines 37-40 and column 18, lines 6-8; each oligonucleotide probe comprises sequences that include at least 20-40 consecutive nucleotides column 6, lines 51-61; included are probes which can hybridize to SEQ ID NO: 3 or complementary sequences thereof, which is 67% homologous to SEQ ID NO: 1727 of Doucette-Stamm and to SEQ ID NO: 5 or complementary sequences thereof, which is 100% homologous to positions 2867-2888 of SEQ ID NO: 1652 of Doucette-Stamm in the rpoB gene of *B. subtilis.;* these probes contain regions that can hybridize to complementary regions of other members of SEQ ID NOS: 1-19 under non-stringent conditions).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 10 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doucette-Stamm et al. (U.S. Patent No. 6,800,744) in view of Remacle et al. (U.S. Patent Pub. No. 2002/0106646).

Doucette-Stamm teaches the limitations of claims 1-9, 15 and 17-22, as discussed above. However, Doucette-Stamm does not teach a diagnostic method wherein DNA microarray technology is used for detecting the formation of a possible hybridization complex, wherein the DNA microarray technology comprises known nucleotide sequences attached in a predetermined order to a small substrate.

Remacle teaches a method for identification of microorganisms based on detection of their homologous nucleotide sequences after hybridization to capture oligonucleotides bound to a microarray (see Abstract, paragraph 16, lines 1-18 and Figure 1). Remacle teaches arrays having from 4 to over 10,000 different single-stranded capture nucleotide sequences/cm^2 of microarray surface (paragraph 29, lines 1-20), for capture of specific amplification products that may be present in a mixture of amplified targets, produced using common primers, using capture nucleotide sequences specific for different species (paragraph 31, lines 1-18), such as *Staphylococcus* species (paragraph 58, lines 1-10).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Doucette-Stamm for detection of bacterial targets such as species of the genus *Streptococcus* using various methods comprising capture probes and the methods of Remacle, who also teaches methods of detecting bacterial targets such as those of *Streptococcus,* using capture oligonucleotides bound to microarrays. Thus, an ordinary practitioner would have been motivated to combine the methods of Doucette-Stamm and Remacle since both teach methods for detection and identification of specific bacterial species, including methods that involve amplification of different members of a genus using common primers and detection of specific species of the genus using capture probes bound to a solid surface. Remacle teaches a method that provides an improved method of microarray analysis for detection of a large number of microorganisms having homologous nucleotide sequences in the FemA gene (Remacle, paragraph 11, lines 1-6), wherein specific target sequences can be identified and recorded at a single spot of the array based on specific binding to capture sequences linked to the surface through a spacer sequence (Remacle, paragraph 12, lines 1-9 and paragraph 18, lines 1-9). Doucette-Stamm teaches a number of different sequences that can be used for detecting bacterial targets (Doucette-Stamm, column 10, line 66 to column 11, line 16 and Table 2), including the rpoB gene target, which can easily be adapted to the microarray system of Remacle.

Response to Arguments

8. Applicant's arguments filed February 18, 2009 have been fully considered but are not fully persuasive.

Applicant argues that the rejection of claims 1, 4, 5, 10 and 15 under 35 USC § 112, second paragraph should be withdrawn based on amendments to the claims. The Examiner agrees and therefore the rejection is withdrawn.

Applicant further argues that the rejection of claims 1-10 and 15 under 35 USC § 102(e) should be withdrawn since the effective 102(e) date of the prior art of Drancourt et al. (U.S. Patent Pub. No. 2006/0199182) does not precede the priority date of the instant application. The Examiner agrees and this rejection is withdrawn. However, upon further search, additional prior art references were identified that anticipate or make obvious the claims as amended (see above).

Conclusion

9. Claims 1-10, 15 and 17-23 are rejected. No claims are allowable.

Correspondence

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David C Thomas/
Examiner, Art Unit 1637

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637